

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 28 JAN 2004

WIPO PCT

Applicant's or agent's file reference TM1-PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/DK 02/00419	International filing date (day/month/year) 20.06.2002	Priority date (day/month/year) 20.06.2001
International Patent Classification (IPC) or both national classification and IPC C12N15/10		
Applicant NUEVOLUTION AS et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 11 sheets, including this cover sheet.  
  
☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  
  
 These annexes consist of a total of 27 sheets.



EPO - DG 1

27.02.2004

- This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

(104)

Date of submission of the demand  15.01.2003	Date of completion of this report  28.01.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer  Hornig, H  Telephone No. +31 70 340-2620  

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/DK 02/00419

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-322 as originally filed

**Claims, Numbers**

1-143 received on 08.12.2003 with letter of 04.12.2003

**Drawings, Sheets**

1/100-100/100 as originally filed

**Sequence listing part of the description, pages:**

1-15, filed with the letter of 07.03.2003,

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☒ furnished subsequently to this Authority in written form.  
☒ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☒ the claims, Nos.: 144-288  
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 133-146

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 133-143

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees, the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

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☒ not complied with for the following reasons:

**see separate sheet**

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1-132 .

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	28-39,84-124
	No: Claims	1-26, 40-83,125-132
Inventive step (IS)	Yes: Claims	28-39,84-124
	No: Claims	1-27,40-83,125-132
Industrial applicability (IA)	Yes: Claims	1-132
	No: Claims	

2. Citations and explanations

**see separate sheet**

**Re Item I**

**Basis of the report**

1.1 The amended claims 1-143 filed with the letter dated 04.12.2003 and received on 08.12.2003 are allowable according to Art. 34(2)(b).

**Re Item IV**

**Lack of unity of invention**

1.1 After reconsidering the application and although the **amended** claims 1-143 have been drafted as being dependent on claim 1, they are clearly defined as **three** different categories of independent subject-matter and have to be subdivided into at least **three** different inventions.

Due to the fact that (i) alternative methods for producing a composition of templated molecules using a plurality of templates (**D2, D7**), (ii) composition of templated molecules per se comprising a plurality of different templated molecules (**D5, D6, D7**) and (iii) screening methods for composition of molecules having a predetermined activity are already state of the art (**D6, D7**), the examining Division therefore confirms the objection put forward by the Search Division as to lack of unity (Art. 13.1 PCT), as reasoned in the International Search Report.

Due to the essential differences of the problem and the provided 3 different solutions and due to the fact that no other technical features can be distinguished which, in the light of the prior art, could be regarded as special technical features common to these solutions, there is no single inventive concept underlying the plurality of claimed inventions of the present application in the sense of Rule 13.1 PCT. Consequently there is lack of unity and three different inventions, not belonging to a common inventive concept.

1. A method for synthesising a composition of templated molecules (claims 1-125),
2. A composition of templated molecules comprising a plurality of different templated molecules (claims 126-132),
3. A method for screening a compositions of molecules having a predetermined activity

(claims 133-143).

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**Citations**

- D1: WO 02 074929 A (KANAN MATTEW W; GARTNER ZEV J ; LIU DAVID R (US); HARVARD COLLEGE ( ) 26 September 2002 (2002-09-26)
- D2: WO 00 61775 A (SERGEEV PAVEL) 19 October 2000 (2000-10-19)
- D3: WALDER J A ET AL: 'COMPLEMENTARY CARRIER PEPTIDE SYNTHESIS: GENERAL STRATEGY AND IMPLICATIONS FOR PREBIOTIC ORIGIN OF PEPTIDE SYNTHESIS' PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 76, no. 1, January 1979 (1979-01), pages 51-55, XP000857351 ISSN: 0027-8424
- D4: KEILER K C ET AL: 'ROLE OF A PEPTIDE TAGGING SYSTEM IN DEGRADATION OF PROTEINS SYNTHESIZED FROM DAMAGED MESSENGER RNA' SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 271, 16 February 1996 (1996-02-16), pages 990-993, XP002041752 ISSN: 0036-8075
- D5: DE 196 46 372 C (EVOTEC BIOSYSTEMS GMBH) 19 June 1997 (1997-06-19)
- D6: WO 93 03172 A (UNIV RESEARCH CORP) 18 February 1993 (1993-02-18) cited in the application
- D7: BRENNER S ET AL: 'ENCODED COMBINATORIAL CHEMISTRY' PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 89, no. 12, 1 June 1992 (1992-06-01), pages 5381-5383, XP000647936 ISSN: 0027-8424

## **2.1 Clarity (Art. 6 PCT)**

2.1.1 Claims 1-132 of subject-matter lack clarity, since the plurality of dependent claims which result makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection. Hence, claims 1-132 do not meet the requirements of Article 6 PCT.

In order to overcome this objection, it would appear appropriate to file an amended set of claims defining the relevant subject-matter and in terms of a **minimum** number of claims (Rule 6.4 PCT).

2.1.2 Furthermore claims 1-132 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem (e.g. attached to a solid or semi-solid support (claim 7); morpholinos sequences, including any analog or derivative thereof (claim 8); template is amplifiable (claim 10); capable of binding an oligonucleotide (claim 14); an anchorage point (claim 15)). The technical features necessary for achieving this result should be added. Moreover, it is not clear what is meant with "reactive group type I", respectively the difference between reactive group type I and II in claims 82-84.

2.1.3 According to the applicant in his letter dated 04.12.2003, the problem underlying the amended claim 1 may be formulated as a provision of a method for producing a composition of compounds from which a sub-composition can be selected by a suitable screening method. It is clear from said statement and from the description and the examples, that the following feature is essential to the definition of the invention:

(i) a method for synthesising a composition of templated molecules using a plurality of templates having **different** coding elements and/or **different** order of coding elements.

By merely adding the features "a composition of templated molecules" and "a plurality of templates" into claim 1, the scope of the amended claim 1 remains unchanged. In

other words, the introduction of "a composition of templated molecules" and "a plurality of templates" into claim 1, the scope of the amended claim 1 further includes: (i) a method for synthesising a composition of several **unitary** templated molecule of a single type (which means the templated molecules are qualitatively **not** different) and (ii) providing a plurality of **unitary** templates of a single type (which means the templates are qualitatively **not** different).

Since the independent claim 1 does not contain said essential technical feature above, it does not meet the requirement of Art. 6 PCT.

## **2.2 Novelty (Art. 33(2) PCT)**

2.2.1 Although **D1** is no prior art within the meaning of Rule 64.1 PCT, it could become important when the application enters the regional phase before the EPO at a later stage because **D1** describes methods of synthesizing chemical compounds by hybridizing one or more templates which have associated reactive unit, with one or more transfer units having anti-codon and reactive unit, and performing reaction of reactive units. Said synthesis comprises one or more chemical compounds, involves providing one or more templates, which optionally have a reactive unit associated with them; and contacting one or more transfer units having an anti-codon and reactive unit with the one or more templates under conditions to allow for hybridization of the one or more anti-codons to template, and reaction of the reactive units.

2.2.2 **D2** describes a process for the synthesis of biologically active compounds (BACs) from inactive precursors (PBACs) 'A', 'B' and 'PAn,' chemically bound to the 5' and/or 3' end of oligomers directly in the cells of living organisms. The method is based on the hybridization of two or more oligonucleotides bound with biologically active substances to specific RNA or DNA. After hybridization of the oligomers to RNA or DNA, the biologically active precursors bound to the 5'/3' ends of the oligomers can interact with each other to make a biologically active form of the substances. Therefore the teaching of **D2** lies within the scope of the first category of claims. In the light of **D2**, the subject-matters of the claims 1-26, 40-83, 125-132 lack novelty.

2.2.3 **D3** describes a method for peptide synthesis based on a template-directed scheme that parallels that of the native ribosomal mechanism. In this procedure,



peptide bond formation is facilitated by the juxtaposition of aminoacyl and peptidyl oligonucleotide carriers bound adjacent to one another on an oligonucleotide template. The scheme provides an intrinsic mechanism by which oligonucleotides can direct the synthesis of polypeptides without protein or ribosomal machinery. In the light of **D3**, the subject-matter of the claims: 1-26, 40-83 and 125-132 lacks novelty.

2.2.4 **D5** describes compounds which comprise a structural unit A (genotype) and a further structural unit B (phenotype), in which the genotype and phenotype are permanently linked to each other, where structural unit A exhibits, besides other regions, at least 1 region coding for at least 1 polymeric molecule constructed from amino acid units and the coding regions are translatable, and furthermore a first structural subunit (terminator) is located in an untranslated section of structural unit A, which permanently links structural unit B as a translation product of structural A to structural unit A. In the light of **D5**, the subject-matter of the claims: 126-132 lacks novelty.

2.2.5 **D6** describes polypeptide ligands of target molecules wherein candidate mixtures comprised of ribosome complexes or mRNA. polypeptide copolymers are partitioned relative to their affinity to the target and amplified to create a new candidate mixture enriched in ribosome complexes or mRNA. polypeptide copolymers with an affinity to the target. In the light of **D6**, the subject-matter of the claims: 126-132 lacks novelty.

2.2.6 **D7** describes a bifunctional molecule of formula A-B-C is claimed, where A = a chemical moiety, B = a linker molecule operatively linked to A and C, C = an identifier oligonucleotide comprising a sequence of nucleotides which identifies the structure of chemical moiety A. In the light of **D7**, the subject-matter of the claims: 126-132 lacks novelty.

### **2.3 Inventive step (Art. 33(3) PCT)**

2.3.1 Due to the fact of complexity and clarity presented under point 2.1 regarding the detailed subject-matter of the claims, it would be a difficult task to give an exact opinion on novelty. Nevertheless, even if some of the subject-matter of claims 1-26, 40-83 and 125-132 could be regarded as new, the subject-matter of said claims lacks an inventive

step under Art. 33(3) PCT.

2.3.2 **D4** describes the role of a peptide tagging system in degradation of proteins synthesised from damaged messenger RNA. A tag is added to the carboxyl terminus of a nascent polypeptide chain by cotranslational switching of the ribosome from the damaged mRNA to ssrA RNA. **D5** describes a compound comprising a structural unit A (genotype) and a further structural unit B (phenotype), in which the genotype and phenotype are permanently linked to each other. Structural unit A exhibits, besides other regions, at least 1 region coding for at least 1 polymeric molecule constructed from amino acid units and the coding regions are translatable, and furthermore a first structural subunit (terminator) is located in an untranslated section of structural unit A, which permanently links structural unit B as a translation product of structural A to structural unit A. **D6** describes a method for preparing polypeptide ligands of target molecules wherein candidate mixtures comprised of ribosome complexes or mRNA.polypeptide copolymers are partitioned relative to their affinity to the target and amplified to create a new candidate mixture enriched in ribosome complexes or mRNA.polypeptide copolymers with an affinity to the target.

Due to the fact that claims 1 contains the **disclaimer**: "...,wherein the synthesis of the templated molecule does not involve ribosome mediated translation of nucleic acid", the synthesis of natural polypeptides (by ribosome mediated translation) falls within the scope of said claim. Therefore in the light of any document **D4 to D6** combined with the general knowledge of a skilled person, the subject-matter of claims 1 and 27 lacks an inventive step under Art. 33(3) PCT.

2.3.3 **D2**, regarded as the closest state of the art, differs from the subject-matter of claims 28-39, that it lacks the essential technical feature of: a method for synthesising a templated molecule, wherein the complementing elements are selected from nucleotides and are linked via a **single protein** which activity is **enzymatically** mediated. In the light of the prior art, the problem of underlying application is the provision of an alternative method of synthesising templated molecules. The solutions as provided by the applicant is a method for synthesising templated molecules, wherein the complementing elements are linked using a **single enzyme**.

2.3.3.1 The combination of the technical features of independent claim 1 with claim 28

is neither known from, nor rendered obvious by, the available prior art. For this reason the subject-matter of claims 28-39 does involve an inventive step and is allowable under Art. 33(3) PCT.

2.3.4 **D2**, regarded as the closest state of the art, differs from the subject-matter of claims 84-124, that it lacks the essential technical feature of: a method for synthesising a templated molecule, wherein each building block comprises two reactive groups. In the light of the prior art, the problem of underlying application is the provision of a further alternative method of synthesising templated molecules. The solutions as provided by the applicant is a method for synthesising templated molecules, wherein the complementing elements are linked via a **non-enzymatically** chemical process and wherein each building block comprises at least two reactive groups.

2.3.4.1 The combination of the technical features of independent claim 1 with claim 84 respectively 85 is neither known from, nor rendered obvious by, the available prior art. For this reason the subject-matter of claims 84-124 does involve an inventive step and is allowable under Art. 33(3) PCT.

## Claims

(47)

1. A method for synthesising a composition of templated molecules comprising a plurality of functional groups, said method comprising the steps of

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i) providing at a plurality of templates comprising a sequence of  $n$  coding elements,

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wherein each coding element comprises at least one recognition group capable of recognising a predetermined complementing element, and

wherein  $n$  is an integer of more than 1,

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ii) providing a plurality of building blocks, wherein each building block comprises

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a) at least one complementing element comprising at least one recognition group capable of recognising a predetermined coding element,

b) at least one functional entity comprising at least one functional group and at least one reactive group, and

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c) at least one linker separating the at least one functional entity from the at least one complementing element,

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iii) contacting each of said coding elements with a complementing element capable of recognising said coding element,

iv) optionally, obtaining a complementing template, and

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v) obtaining a templated molecule comprising covalently linked, functional groups by linking, by means of a reaction involving reactive groups, a functional group of at least one functional entity to a functional group of another, functional entity,

## Claims

(47)

1. A method for synthesising a composition of templated molecules comprising a plurality of functional groups, said method comprising the steps of

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- i) providing at a plurality of templates comprising a sequence of n coding elements,

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wherein each coding element comprises at least one recognition group capable of recognising a predetermined complementing element, and

wherein n is an integer of more than 1,

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- ii) providing a plurality of building blocks, wherein each building block comprises

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- a) at least one complementing element comprising at least one recognition group capable of recognising a predetermined coding element,

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- b) at least one functional entity comprising at least one functional group and at least one reactive group, and

- c) at least one linker separating the at least one functional entity from the at least one complementing element,

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- iii) contacting each of said coding elements with a complementing element capable of recognising said coding element,

- iv) optionally, obtaining a complementing template, and

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- v) obtaining a templated molecule comprising covalently linked, functional groups by linking, by means of a reaction involving reactive groups, a functional group of at least one functional entity to a functional group of another, functional entity,



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wherein the templated molecule is linked by means of a linker to the complementing template or template that templated the synthesis of the templated molecule, and

- 5        wherein the synthesis of the templated molecule does not involve ribosome mediated translation of a nucleic acid.
2. Method of claim 1, wherein the templated molecule is linked by means of a single linker to the complementing template or template that templated the synthesis of the templated molecule.
- 10        3. The method of claim 1, wherein steps iii) through v) are repeated.
4. The method of claim 1, wherein the template comprising n coding elements is a linear sequence of coding elements.
- 15        5. The method of claim 1, wherein the template comprising n coding elements is branched.
- 20        6. The method of claim 1, wherein n preferably has a value of from 2 to 200, for example from 2 to 100, such as from 2 to 80, for example from 2 to 60, such as from 2 to 40, for example from 2 to 30, such as from 2 to 20, for example from 2 to 15, such as from 2 to 10, such as from 2 to 8, for example from 2 to 6, such as from 2 to 4, for example 2, such as from 3 to 100, for example from 3 to 80, such as from 3 to 60, such as from 3 to 40, for example from 3 to 30, such as from 3 to 20, such as from 3 to 15, for example from 3 to 15, such as from 3 to 10, such as from 3 to 8, for example from 3 to 6, such as from 3 to 4, for example 3, such as from 4 to 100, for example from 4 to 80, such as from 4 to 60, such as from 4 to 40, for example from 4 to 30, such as from 4 to 20, such as from 4 to 15, for example from 4 to 10, such as from 4 to 8, such as from 4 to 6, for example 4, for example from 5 to 100, such as from 5 to 80, for example from 5 to 60, such as from 5 to 40, for example from 5 to 30, such as from 5 to 20, for example from 5 to 15, such as from 5 to 10, such as from 5 to 8, for example from 5 to 6, for example 5, such as from 6 to 100, for example from 6 to 80, such as from 6 to 60, such as from 6 to 40, for example from 6 to 30, such
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as from 6 to 20, such as from 6 to 15, for example from 6 to 10, such as from 6 to 8, such as 6, for example from 7 to 100, such as from 7 to 80, for example from 7 to 60, such as from 7 to 40, for example from 7 to 30, such as from 7 to 20, for example from 7 to 15, such as from 7 to 10, such as from 7 to 8, for example 7, for example from 8 to 100, such as from 8 to 80, for example from 8 to 60, such as from 8 to 40, for example from 8 to 30, such as from 8 to 20, for example from 8 to 15, such as from 8 to 10, such as 8, for example 9, for example from 10 to 100, such as from 10 to 80, for example from 10 to 60, such as from 10 to 40, for example from 10 to 30, such as from 10 to 20, for example from 10 to 15, such as from 10 to 12, such as 10, for example from 12 to 100, such as from 12 to 80, for example from 12 to 60, such as from 12 to 40, for example from 12 to 30, such as from 12 to 20, for example from 12 to 15, such as from 14 to 100, such as from 14 to 80, for example from 14 to 60, such as from 14 to 40, for example from 14 to 30, such as from 14 to 20, for example from 14 to 16, such as from 16 to 100, such as from 16 to 80, for example from 16 to 60, such as from 16 to 40, for example from 16 to 30, such as from 16 to 20, such as from 18 to 100, such as from 18 to 80, for example from 18 to 60, such as from 18 to 40, for example from 18 to 30, such as from 18 to 20, for example from 20 to 100, such as from 20 to 80, for example from 20 to 60, such as from 20 to 40, for example from 20 to 30, such as from 20 to 25, for example from 22 to 100, such as from 22 to 80, for example from 22 to 60, such as from 22 to 40, for example from 22 to 30, such as from 22 to 25, for example from 25 to 100, such as from 25 to 80, for example from 25 to 60, such as from 25 to 40, for example from 25 to 30, such as from 30 to 100, for example from 30 to 80, such as from 30 to 60, for example from 30 to 40, such as from 30 to 35, for example from 35 to 100, such as from 35 to 80, for example from 35 to 60, such as from 35 to 40, for example from 40 to 100, such as from 40 to 80, for example from 40 to 60, such as from 40 to 50, for example from 40 to 45, such as from 45 to 100, for example from 45 to 80, such as from 45 to 60, for example from 45 to 50, such as from 50 to 100, for example from 50 to 80, such as from 50 to 60, for example from 50 to 55, such as from 60 to 100, for example from 60 to 80, such as from 60 to 70, for example from 70 to 100, such as from 70 to 90, for example from 70 to 80, such as from 80 to 100, for example from 80 to 90, such as from 90 to 100.

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7. The method of claim 1, wherein the template is attached to a solid or semi-solid support.
- 5 8. The method of claim 1, wherein the template comprises or essentially consists of nucleotides selected from the group consisting of deoxyribonucleic acids (DNA), ribonucleic acids (RNA), peptide nucleic acids (PNA), locked nucleic acids (LNA), and morpholinos sequences, including any analog or derivative thereof.
- 10 9. The method of claim 1, wherein the template comprises or essentially consists of nucleotides selected from the group consisting of DNA, RNA, PNA, LNA and morpholinos sequence, including any analog or derivative thereof, and wherein the complementing element comprises or essentially consists of nucleotides selected from the group consisting of DNA, RNA, PNA, LNA and morpholinos sequence, including any analog or derivative thereof.
- 15 10. The method of claim 1, wherein the template is amplifiable.
- 20 11. The method of claim 10, wherein the single strand of coding elements is capable of forming a double helix by hybridization to a complementing template comprising a single strand of complementing elements.
12. The method of any of claims 1 to 11, wherein the template comprises a priming site.
- 25 13. The method according to claim 12, wherein the priming site is upstream of the coding elements and is capable of binding a primer for initiating the incorporation of building blocks and/or for amplification of the coding elements of the templates.
- 30 14. The method of claim 12, wherein the priming site is downstream of the coding elements and is capable of binding an oligonucleotide.
- 35 15. The method of claim 14, wherein the oligonucleotide comprises an anchorage point, which can bind the templated molecule.

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16. The method according to claim 14, wherein the oligonucleotide is capable of stopping further incorporation of building blocks.

5 17. The method of claim 14, wherein the priming site is capable of binding a reverse primer.

18. The method of claim 1, wherein the coding element preferably comprises or essentially consists of from 1 to 100 subunits, such as from 1 to 80 subunits, for example from 1 to 60 subunits, such as from 1 to 40 subunits, for example from 1 to 20 subunits, such as from 1 to 18 subunits, for example from 1 to 16 subunits, such as from 1 to 14 subunits, for example from 1 to 12 subunits, such as from 1 to 10 subunits, for example from 1 to 9 subunits, such as from 1 to 8 subunits, for example from 1 to 7 subunits, such as from 1 to 6 subunits, for example from 1 to 5 subunits, such as from 1 to 4 subunits, for example from 1 to 3 subunits, such as from 1 to 2 subunits, for example 1 subunit, such as from 2 to 100 subunits, such as from 2 to 80 subunits, for example from 2 to 60 subunits, such as from 2 to 40 subunits, for example from 2 to 20 subunits, such as from 2 to 18 subunits, for example from 2 to 16 subunits, such as from 2 to 14 subunits, for example from 2 to 12 subunits, such as from 2 to 10 subunits, for example from 2 to 9 subunits, such as from 2 to 8 subunits, for example from 2 to 7 subunits, such as from 2 to 6 subunits, for example from 2 to 5 subunits, such as from 2 to 4 subunits, for example from 2 to 3 subunits, such as 2 subunits, such as from 3 to 100 subunits, such as from 3 to 80 subunits, for example from 3 to 60 subunits, such as from 3 to 40 subunits, for example from 3 to 20 subunits, such as from 3 to 18 subunits, for example from 3 to 16 subunits, such as from 3 to 14 subunits, for example from 3 to 12 subunits, such as from 3 to 10 subunits, for example from 3 to 9 subunits, such as from 3 to 8 subunits, for example from 3 to 7 subunits, such as from 3 to 6 subunits, for example from 3 to 5 subunits, such as from 3 to 4 subunits, for example 3 subunits, for example from 4 to 100 subunits, such as from 4 to 80 subunits, for example from 4 to 60 subunits, such as from 4 to 40 subunits, for example from 4 to 20 subunits, such as from 4 to 18 subunits, for example from 4 to 16 subunits, such as from 4 to 14 subunits, for example from 4 to 12 subunits, such as from 4 to 10 subunits, for example from 4 to 9 subunits, such as from 4 to 8 subunits, for example from 4 to 7 subunits, such as from 4 to 6 subunits, for

example from 4 to 5 subunits, for example 4 subunits, such as from 5 to 100 subunits, such as from 5 to 80 subunits, for example from 5 to 60 subunits, such as from 5 to 40 subunits, for example from 5 to 20 subunits, such as from 5 to 18 subunits, for example from 5 to 16 subunits, such as from 5 to 14 subunits, for example from 5 to 12 subunits, such as from 5 to 10 subunits, for example from 5 to 9 subunits, such as from 5 to 8 subunits, for example from 5 to 7 subunits, such as from 5 to 6 subunits, such as 5 subunits, for example from 6 to 100 subunits, such as from 6 to 80 subunits, for example from 6 to 60 subunits, such as from 6 to 40 subunits, for example from 6 to 20 subunits, such as from 6 to 18 subunits, for example from 6 to 16 subunits, such as from 6 to 14 subunits, for example from 6 to 12 subunits, such as from 6 to 10 subunits, for example from 6 to 9 subunits, such as from 6 to 8 subunits, for example from 6 to 7 subunits, such as 6 subunits, such as from 7 to 100 subunits, such as from 7 to 80 subunits, for example from 7 to 60 subunits, such as from 7 to 40 subunits, for example from 7 to 20 subunits, such as from 7 to 18 subunits, for example from 7 to 16 subunits, such as from 7 to 14 subunits, for example from 7 to 12 subunits, such as from 7 to 10 subunits, for example from 7 to 9 subunits, such as from 7 to 8 subunits, such as 7 subunits, for example from 8 to 100 subunits, such as from 8 to 80 subunits, for example from 8 to 60 subunits, such as from 8 to 40 subunits, for example from 8 to 20 subunits, such as from 8 to 18 subunits, for example from 8 to 16 subunits, such as from 8 to 14 subunits, for example from 8 to 12 subunits, such as from 8 to 10 subunits, for example from 8 to 9 subunits, for example 8 subunits, such as from 9 to 100 subunits, such as from 9 to 80 subunits, for example from 9 to 60 subunits, such as from 9 to 40 subunits, for example from 9 to 20 subunits, such as from 9 to 18 subunits, for example from 9 to 16 subunits, such as from 9 to 14 subunits, for example from 9 to 12 subunits, such as from 9 to 10 subunits, such as 9 subunits, for example from 10 to 100 subunits, such as from 10 to 80 subunits, for example from 10 to 60 subunits, such as from 10 to 40 subunits, for example from 10 to 20 subunits, such as from 10 to 18 subunits, for example from 10 to 16 subunits, such as from 10 to 14 subunits, for example from 10 to 12 subunits, such as 10 subunits, such as from 11 to 100 subunits, such as from 11 to 80 subunits, for example from 11 to 60 subunits, such as from 11 to 40 subunits, for example from 11 to 20 subunits, such as from 11 to 18 subunits, for example from 11 to 16 subunits, such as from 11 to 14 subunits, for example from 11 to 12 subunits, such as

from 12 to 100 subunits, such as from 12 to 80 subunits, for example from 12 to 60 subunits, such as from 12 to 40 subunits, for example from 12 to 20 subunits, such as from 12 to 18 subunits, for example from 12 to 16 subunits, such as from 12 to 14 subunits, for example from 13 to 100 subunits, such as from 13 to 80 subunits, for example from 13 to 60 subunits, such as from 13 to 40 subunits, for example from 13 to 20 subunits, such as from 13 to 18 subunits, for example from 13 to 16 subunits, such as from 13 to 14 subunits, for example from 14 to 100 subunits, such as from 14 to 80 subunits, for example from 14 to 60 subunits, such as from 14 to 40 subunits, for example from 14 to 20 subunits, such as from 14 to 18 subunits, for example from 14 to 16 subunits, such as from 15 to 100 subunits, such as from 15 to 80 subunits, for example from 15 to 60 subunits, such as from 15 to 40 subunits, for example from 15 to 20 subunits, such as from 15 to 18 subunits, for example from 15 to 16 subunits, such as from 16 to 100 subunits, such as from 16 to 80 subunits, for example from 16 to 60 subunits, such as from 16 to 40 subunits, for example from 16 to 20 subunits, such as from 16 to 18 subunits, for example from 17 to 100 subunits, such as from 17 to 80 subunits, for example from 17 to 60 subunits, such as from 17 to 40 subunits, for example from 17 to 20 subunits, such as from 17 to 18 subunits, for example from 18 to 100 subunits, such as from 18 to 80 subunits, for example from 18 to 60 subunits, such as from 18 to 40 subunits, for example from 18 to 20 subunits, such as from 19 to 100 subunits, such as from 19 to 80 subunits, for example from 19 to 60 subunits, such as from 19 to 40 subunits, for example from 19 to 30 subunits, such as from 19 to 25 subunits, for example from 20 to 100 subunits, such as from 20 to 80 subunits, for example from 20 to 60 subunits, such as from 20 to 40 subunits, for example from 20 to 30 subunits, such as from 20 to 25 subunits.

19. The method of claim 18, wherein each subunit comprises or essentially consists of a nucleotide, or a nucleotide analog.
20. The method of claim 1, wherein the complementing template comprising n complementing elements is a linear sequence of coding elements.
21. The method of claim 1, wherein the complementing template comprising n complementing elements is branched.

22. The method of any of claims 20 and 21, wherein n preferably has a value of from 2 to 200, for example from 2 to 100, such as from 2 to 80, for example from 2 to 60, such as from 2 to 40, for example from 2 to 30, such as from 2 to 20, for example from 2 to 15, such as from 2 to 10, such as from 2 to 8, for example from 2 to 6, such as from 2 to 4, such as 2, such as from 3 to 100, for example from 3 to 80, such as from 3 to 60, such as from 3 to 40, for example from 3 to 30, such as from 3 to 20, such as from 3 to 15, for example from 3 to 15, such as from 3 to 10, such as from 3 to 8, for example from 3 to 6, such as from 3 to 4, for example 3, such as from 4 to 100, for example from 4 to 80, such as from 4 to 60, such as from 4 to 40, for example from 4 to 30, such as from 4 to 20, such as from 4 to 15, for example from 4 to 10, such as from 4 to 8, such as from 4 to 6, such as 4, for example from 5 to 100, such as from 5 to 80, for example from 5 to 60, such as from 5 to 40, for example from 5 to 30, such as from 5 to 20, for example from 5 to 15, such as from 5 to 10, such as from 5 to 8, for example from 5 to 6, for example 5, such as from 6 to 100, for example from 6 to 80, such as from 6 to 60, such as from 6 to 40, for example from 6 to 30, such as from 6 to 20, such as from 6 to 15, for example from 6 to 10, such as from 6 to 8, such as 6, for example from 7 to 100, such as from 7 to 80, for example from 7 to 60, such as from 7 to 40, for example from 7 to 30, such as from 7 to 20, for example from 7 to 15, such as from 7 to 10, such as from 7 to 8, such as 7, for example from 8 to 100, such as from 8 to 80, for example from 8 to 60, such as from 8 to 40, for example from 8 to 30, such as from 8 to 20, for example from 8 to 15, such as from 8 to 10, for example 8, such as 9, for example from 10 to 100, such as from 10 to 80, for example from 10 to 60, such as from 10 to 40, for example from 10 to 30, such as from 10 to 20, for example from 10 to 15, such as from 10 to 12, such as 10, for example from 12 to 100, such as from 12 to 80, for example from 12 to 60, such as from 12 to 40, for example from 12 to 30, such as from 12 to 20, for example from 12 to 15, such as from 14 to 100, such as from 14 to 80, for example from 14 to 60, such as from 14 to 40, for example from 14 to 30, such as from 14 to 20, for example from 14 to 16, such as from 16 to 100, such as from 16 to 80, for example from 16 to 60, such as from 16 to 40, for example from 16 to 30, such as from 16 to 20, such as from 18 to 100, such as from 18 to 80, for example from 18 to 60, such as from 18 to 40, for example from 18 to 30, such as from 18 to 20, for

example from 20 to 100, such as from 20 to 80, for example from 20 to 60, such as from 20 to 40, for example from 20 to 30, such as from 20 to 25, for example from 22 to 100, such as from 22 to 80, for example from 22 to 60, such as from 22 to 40, for example from 22 to 30, such as from 22 to 25, for example from 25 to 100, such as from 25 to 80, for example from 25 to 60, such as from 25 to 40, for example from 25 to 30, such as from 30 to 100, for example from 30 to 80, such as from 30 to 60, for example from 30 to 40, such as from 30 to 35, for example from 35 to 100, such as from 35 to 80, for example from 35 to 60, such as from 35 to 40, for example from 40 to 100, such as from 40 to 80, for example from 40 to 60, such as from 40 to 50, for example from 40 to 45, such as from 45 to 100, for example from 45 to 80, such as from 45 to 60, for example from 45 to 50, such as from 50 to 100, for example from 50 to 80, such as from 50 to 60, for example from 50 to 55, such as from 60 to 100, for example from 60 to 80, such as from 60 to 70, for example from 70 to 100, such as from 70 to 90, for example from 70 to 80, such as from 80 to 100, for example from 80 to 90, such as from 90 to 100.

23. The method of claim 1, wherein the complementing template is attached to a solid or semi-solid support.
24. The method of claim 1, wherein the complementing elements are selected from the group consisting of nucleotides, nucleotide derivatives and nucleotide analogs in which one or more of a base moiety and/or a phosphate moiety and/or a ribose and/or a deoxyribose moiety has been substituted by an alternative molecular entity.
25. The method of claim 1, wherein the complementing element preferably comprises or essentially consists of from 1 to 100 subunits, such as from 1 to 80 subunits, for example from 1 to 60 subunits, such as from 1 to 40 subunits, for example from 1 to 20 subunits, such as from 1 to 18 subunits, for example from 1 to 16 subunits, such as from 1 to 14 subunits, for example from 1 to 12 subunits, such as from 1 to 10 subunits, for example from 1 to 9 subunits, such as from 1 to 8 subunits, for example from 1 to 7 subunits, such as from 1 to 6 subunits, for example from 1 to 5 subunits, such as from 1 to 4 subunits, for example from 1 to 3 subunits, such as from 1 to 2 subunits, for example 1

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subunit, such as from 2 to 100 subunits, such as from 2 to 80 subunits, for example from 2 to 60 subunits, such as from 2 to 40 subunits, for example from 2 to 20 subunits, such as from 2 to 18 subunits, for example from 2 to 16 subunits, such as from 2 to 14 subunits, for example from 2 to 12 subunits, such as from 2 to 10 subunits, for example from 2 to 9 subunits, such as from 2 to 8 subunits, for example from 2 to 7 subunits, such as from 2 to 6 subunits, for example from 2 to 5 subunits, such as from 2 to 4 subunits, for example from 2 to 3 subunits, such as 2 subunits, such as from 3 to 100 subunits, such as from 3 to 80 subunits, for example from 3 to 60 subunits, such as from 3 to 40 subunits, for example from 3 to 20 subunits, such as from 3 to 18 subunits, for example from 3 to 16 subunits, such as from 3 to 14 subunits, for example from 3 to 12 subunits, such as from 3 to 10 subunits, for example from 3 to 9 subunits, such as from 3 to 8 subunits, for example from 3 to 7 subunits, such as from 3 to 6 subunits, for example from 3 to 5 subunits, such as from 3 to 4 subunits, for example 3 subunits, for example from 4 to 100 subunits, such as from 4 to 80 subunits, for example from 4 to 60 subunits, such as from 4 to 40 subunits, for example from 4 to 20 subunits, such as from 4 to 18 subunits, for example from 4 to 16 subunits, such as from 4 to 14 subunits, for example from 4 to 12 subunits, such as from 4 to 10 subunits, for example from 4 to 9 subunits, such as from 4 to 8 subunits, for example from 4 to 7 subunits, such as from 4 to 6 subunits, for example from 4 to 5 subunits, for example 4 subunits, such as from 5 to 100 subunits, such as from 5 to 80 subunits, for example from 5 to 60 subunits, such as from 5 to 40 subunits, for example from 5 to 20 subunits, such as from 5 to 18 subunits, for example from 5 to 16 subunits, such as from 5 to 14 subunits, for example from 5 to 12 subunits, such as from 5 to 10 subunits, for example from 5 to 9 subunits, such as from 5 to 8 subunits, for example from 5 to 7 subunits, such as from 5 to 6 subunits, such as 5 subunits, for example from 6 to 100 subunits, such as from 6 to 80 subunits, for example from 6 to 60 subunits, such as from 6 to 40 subunits, for example from 6 to 20 subunits, such as from 6 to 18 subunits, for example from 6 to 16 subunits, such as from 6 to 14 subunits, for example from 6 to 12 subunits, such as from 6 to 10 subunits, for example from 6 to 9 subunits, such as from 6 to 8 subunits, for example from 6 to 7 subunits, such as 6 subunits, such as from 7 to 100 subunits, such as from 7 to 80 subunits, for example from 7 to 60 subunits, such as from 7 to 40 subunits, for example from 7 to 20 subunits, such as from 7 to 18

subunits, for example from 7 to 16 subunits, such as from 7 to 14 subunits, for example from 7 to 12 subunits, such as from 7 to 10 subunits, for example from 7 to 9 subunits, such as from 7 to 8 subunits, such as 7 subunits, for example from 8 to 100 subunits, such as from 8 to 80 subunits, for example from 8 to 60 subunits, such as from 8 to 40 subunits, for example from 8 to 20 subunits, such as from 8 to 18 subunits, for example from 8 to 16 subunits, such as from 8 to 14 subunits, for example from 8 to 12 subunits, such as from 8 to 10 subunits, for example from 8 to 9 subunits, for example 8 subunits, such as from 9 to 100 subunits, such as from 9 to 80 subunits, for example from 9 to 60 subunits, such as from 9 to 40 subunits, for example from 9 to 20 subunits, such as from 9 to 18 subunits, for example from 9 to 16 subunits, such as from 9 to 14 subunits, for example from 9 to 12 subunits, such as from 9 to 10 subunits, such as 9 subunits, for example from 10 to 100 subunits, such as from 10 to 80 subunits, for example from 10 to 60 subunits, such as from 10 to 40 subunits, for example from 10 to 20 subunits, such as from 10 to 18 subunits, for example from 10 to 16 subunits, such as from 10 to 14 subunits, for example from 10 to 12 subunits, such as 10 subunits, such as from 11 to 100 subunits, such as from 11 to 80 subunits, for example from 11 to 60 subunits, such as from 11 to 40 subunits, for example from 11 to 20 subunits, such as from 11 to 18 subunits, for example from 11 to 16 subunits, such as from 11 to 14 subunits, for example from 11 to 12 subunits, such as from 12 to 100 subunits, such as from 12 to 80 subunits, for example from 12 to 60 subunits, such as from 12 to 40 subunits, for example from 12 to 20 subunits, such as from 12 to 18 subunits, for example from 12 to 16 subunits, such as from 12 to 14 subunits, for example from 13 to 100 subunits, such as from 13 to 80 subunits, for example from 13 to 60 subunits, such as from 13 to 40 subunits, for example from 13 to 20 subunits, such as from 13 to 18 subunits, for example from 13 to 16 subunits, such as from 13 to 14 subunits, for example from 14 to 100 subunits, such as from 14 to 80 subunits, for example from 14 to 60 subunits, such as from 14 to 40 subunits, for example from 14 to 20 subunits, such as from 14 to 18 subunits, for example from 14 to 16 subunits, such as from 15 to 100 subunits, such as from 15 to 80 subunits, for example from 15 to 60 subunits, such as from 15 to 40 subunits, for example from 15 to 20 subunits, such as from 15 to 18 subunits, for example from 15 to 16 subunits, such as from 16 to 100 subunits, such as from 16 to 80 subunits, for example from 16 to 60 subunits, such as from 16 to 40 subunits, for



example from 16 to 20 subunits, such as from 16 to 18 subunits, for example from 17 to 100 subunits, such as from 17 to 80 subunits, for example from 17 to 60 subunits, such as from 17 to 40 subunits, for example from 17 to 20 subunits, such as from 17 to 18 subunits, for example from 18 to 100 subunits, such as from 18 to 80 subunits, for example from 18 to 60 subunits, such as from 18 to 40 subunits, for example from 18 to 20 subunits, such as from 19 to 100 subunits, such as from 19 to 80 subunits, for example from 19 to 60 subunits, such as from 19 to 40 subunits, for example from 19 to 30 subunits, such as from 19 to 25 subunits, for example from 20 to 100 subunits, such as from 20 to 80 subunits, for example from 20 to 60 subunits, such as from 20 to 40 subunits, for example from 20 to 30 subunits, such as from 20 to 25 subunits.

26. The method of claim 89, wherein each subunit comprises or essentially consists of a nucleotide, or a nucleotide analog.

27. The method of claim 1, wherein the complementing elements are selected from nucleotides, and the complementing elements are linked enzymatically.

28. The method according to claim 27, wherein the enzyme is selected from the group consisting of template-dependent DNA- and RNA-polymerases, including reverse transcriptases, DNA-ligases and RNA-ligases, ribozymes and deoxyribozymes, including HIV-1 Reverse Transcriptase, AMV Reverse Transcriptase, T7 RNA polymerase, T7 RNA polymerase mutant Y639F, Sequenase, Taq DNA polymerase, Klenow Fragment (Large fragment of DNA polymerase I), DNA-ligase, T7 DNA polymerase, T4 DNA polymerase, T4 DNA Ligase, E. coli RNA polymerase, rTh DNA polymerase, Vent DNA polymerase, Pfu DNA polymerase, Tte DNA polymerase, repair polymerase, and ribozymes with ligase or replicase activities.

29. The method of claim 28, wherein the enzyme is selected from the group consisting of HIV-1 Reverse Transcriptase, AMV Reverse Transcriptase, T7 RNA polymerase, T7 RNA polymerase mutant Y639F, Sequenase, Taq DNA polymerase, Klenow Fragment (Large fragment of DNA polymerase I), DNA-ligase, T7 DNA polymerase, T4 DNA polymerase, and T4 DNA Ligase.

30. The method of any of claims 27 to 29, wherein the nucleotides form a complementing template upon incorporation.
- 5 31. The method according to any of the claim 27 to 30, wherein a primer is annealed to a priming site on the template and a suitable polymerase or transcriptase extends the primer by incorporation of building blocks to obtain a complementing template.
- 10 32. The method according to claim 31, wherein the building block is a mono-, di- or oligonucleotide derivative.
33. The method according to claim 32, wherein the building block is a mononucleotide derivative.
- 15 34. The method according to any of the claims 32 to 33, wherein the functional entity is attached to the nucleobase moiety through a linker.
35. The method according to claim 34, wherein the linker comprises a triple bond.
- 20 36. The method according to any of the claims 31 to 35, wherein the building block is designed such that the functional entity protrudes into the major groove of a nucleic acid helix, when incorporated in a complementing template.
- 25 37. The method according to any of the claims 27 to 29, wherein the complementing elements are selected from oligonucleotides and the complementing elements are linked enzymatically using a ligase.
- 30 38. The method according to claim 37, wherein the complementing element oligonucleotides each comprise three or more nucleic acid monomers.
- 35 39. The method according to claim 38, wherein the complementing element is an oligonucleotide comprising 4 to 100 nucleic acid monomers.
40. The method according to claim 1, wherein a complementing element anneals to the coding element, without being coupled to another complementing element.

41. The method according to claim 40, wherein the complementing element comprises an oligonucleotide of 6 to 100 nucleotide monomers.

5      42. The method according to claim 41, wherein the oligonucleotide comprises 10 to 50 nucleotide monomers.

43. The method according to any of the claims 37 to 42, wherein the length of the linker is at least half the length of the complementing element.

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44. The method according to any of the claims 37 to 43, wherein the linker comprises an oligonucleotide.

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45. The method according to any of the claims 41 to 44, wherein the oligonucleotide complementing element and the oligonucleotide linker is a continuous oligonucleotide.

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46. The method according to any of the claims 44 to 45, wherein two linkers of distinct building blocks each comprises one part of a molecule pair, said pair being capable of reversible interaction.

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47. The method according to claim 46, wherein the molecule pair comprises a double stranded sequence of nucleic acids forming a dimerisation domain on the linkers.

48. The method according to claim 46 or 47, wherein the dimerisation domain part of a linker is proximal to the functional entity.

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49. The method according to claim 47 or 48, wherein the sequence of nucleic acids monomers forming the one part of the molecule pair is separated with 2, 1, or 0 nucleic acid monomers from the functional entity.

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50. The method according to claim 49, wherein the functional entity is directly attached to the dimerisation domain.

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51. The method according to any of the claims 44 to 50, wherein the sequence of nucleic acid monomers comprises 3 to 20 mononucleic acids.
52. The method according to claim 51, wherein the sequence comprises 3 to 15 nucleic acid monomers.
53. The method according to claim 52, wherein the sequence comprises 4 to 12 nucleic acid monomers.
54. The method according to any of the claims 37 to 53, wherein the functional entity is attached to a nucleobase of the oligonucleotide linker.
55. The method according to claim 54, wherein the functional entity is attached to a terminal nucleotide of the linker.
56. The method of claim 1, wherein the complementing elements are selected from nucleotides, and the complementing elements are linked by using a chemical agent, pH change, light, a catalyst, radiation, such as electromagnetic radiation, or by spontaneous coupling when being brought into reactive contact with each other.
57. The method according to claim 56, wherein the chemical agent comprises a phosphoimidazolid group.
58. The method according to claim 56 and 57, wherein the phosphoimidazolid group is attached to the 5' end of the building block and the building block is linked to a nascent complementing template at the 3' hydroxyl group thereof.
59. Method of claim 1, wherein at least a subset of said plurality of building blocks preferably comprises one complementing element and/or one functional entity and/or one linker.
60. The method of claim 1, wherein a subset of said plurality of building blocks comprises a selectively cleavable linker separating the functional entity from the complementing element, wherein said selectively cleavable linker is not cleaved

under conditions resulting in cleavage of cleavable linkers separating the functional entity from the complementing element of building blocks not belonging to the subset of building blocks comprising a selectively cleavable linker.

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61. The method according to claim 60, wherein the functional entity is released by cleaving the cleavable linkers such that no trace of the linker appears on the functional entity.

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62. The method of claim 60 or 61, wherein the cleavable linkers are cleaved, and wherein the at least one selectively cleavable linker is not cleaved, and wherein the templated molecule is linked to the template and/or to the complementing element by means of said at least one selectively cleavable linker.

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63. The method of claims 60 to 62, wherein the linkers are cleaved by acid, base, a chemical agent, light, electromagnetic radiation, an enzyme, or a catalyst.

64. The method according to claim 63, wherein the linker cleaved by light comprises a nitrophenyl moiety.

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65. The method of claim 1, wherein the length of the linker or selectively cleavable linker is in the range of from about 0.8 Å to about 70 Å, such as in the range of from 0.8 Å to about 60 Å, for example in the range of from 0.8 Å to about 50 Å, such as in the range of from 0.8 Å to about 40 Å, for example in the range of from 0.8 Å to about 30 Å, such as in the range of from 0.8 Å to about 25 Å, for example in the range of from 0.8 Å to about 20 Å, such as in the range of from 0.8 Å to about 18 Å, for example in the range of from 0.8 Å to about 16 Å, such as in the range of from 0.8 Å to about 14 Å, for example in the range of from 0.8 Å to about 12 Å, such as in the range of from 0.8 Å to about 10 Å, for example in the range of from 0.8 Å to about 8 Å, such as in the range of from 0.8 Å to about 7 Å, for example in the range of from 0.8 Å to about 6 Å, such as in the range of from 0.8 Å to about 5 Å, for example in the range of from 0.8 Å to about 4 Å, such as in the range of from 0.8 Å to about 3.5 Å, for example in the range of from 0.8 Å to about 3.0 Å, such as in the range of from 0.8 Å to about 2.5 Å, for

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example in the range of from 0.8 Å to about 2.0 Å, such as in the range of from 0.8 Å to about 1.5 Å, for example in the range of from 0.8 Å to about 1.0 Å.

66. The method of claim 1, wherein the length of the linker or selectively cleavable linker is in the range of from about 6 Å to about 40 Å, such as in the range of from 6 Å to about 30 Å, such as in the range of from 6 Å to about 25 Å, for example in the range of from 6 Å to about 20 Å, such as in the range of from 6 Å to about 18 Å, for example in the range of from 6 Å to about 16 Å, such as in the range of from 6 Å to about 14 Å, for example in the range of from 6 Å to about 12 Å, such as in the range of from 6 Å to about 10 Å, for example in the range of from 6 Å to about 8 Å, such as in the range of from 6 Å to about 7 Å.

67. The method of claim 1, wherein the length of the linker or selectively cleavable linker is in the range of from about 8 Å to about 40 Å, such as in the range of from 8 Å to about 30 Å, such as in the range of from 8 Å to about 25 Å, for example in the range of from 8 Å to about 20 Å, such as in the range of from 8 Å to about 18 Å, for example in the range of from 8 Å to about 16 Å, such as in the range of from 8 Å to about 14 Å, for example in the range of from 8 Å to about 12 Å, such as in the range of from 8 Å to about 10 Å.

68. The method according to claim 1, wherein the obtained templated molecule comprises a sequence of covalently linked functional groups, by means of a reaction involving reactive groups, a functional group of at least one functional entity to a functional group of a neighbouring functional entity.

69. The method according to any of the claims 1 to 68, wherein the templated molecule is a linear sequence of functional groups.

70. The method according to any of the claims 1 to 69, wherein the templated molecule is a branched sequence of functional groups.

71. The method according to any of the claims 1 to 69, wherein the templated molecule is a cyclic sequence of functional groups.

72. The method of claim 1, wherein the templated molecule comprises or essentially consists of molecules or molecular entities selected from the group of  $\alpha$ -

peptides,  $\beta$ -peptides,  $\gamma$ -peptides,  $\omega$ -peptides, mono-, di- and tri-substituted  $\alpha$ -peptides,  $\beta$ -peptides,  $\gamma$ -peptides,  $\omega$ -peptides, peptides wherein the amino acid residues are in the L-form or in the D-form, vinylogous polypeptides, glycopolypeptides, polyamides, vinylogous sulfonamide peptide, polysulfonamide, conjugated peptides comprising e.g. prosthetic groups, polyesters, polysaccharides, polycarbamates, polycarbonates, polyureas, polypeptidylphosphonates, polyurethanes, azatides, oligo N-substituted glycines, polyethers, ethoxyformacetal oligomers, poly-thioethers, polyethylene glycols (PEG), polyethylenes, polydisulfides, polyarylene sulfides, polynucleotides, PNAs, LNAs, morpholinos, oligo pyrrolinone, polyoximes, polyimines, polyethyleneimines, polyimides, polyacetals, polyacetates, polystyrenes, polyvinyl, lipids, phospholipids, glycolipids, polycyclic compounds comprising e.g. aliphatic or aromatic cycles, including polyheterocyclic compounds, proteoglycans, and polysiloxanes, including any combination thereof.

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73. The method of claim 1, wherein neighbouring residues of the templated molecule is linked by a chemical bond selected from the group of chemical bonds consisting of peptide bonds, sulfonamide bonds, ester bonds, saccharide bonds, carbamate bonds, carbonate bonds, urea bonds, phosphonate bonds, urethane bonds, azatide bonds, peptoid bonds, ether bonds, ethoxy bonds, thioether bonds, single carbon bonds, double carbon bonds, triple carbon bonds, disulfide bonds, sulfide bonds, phosphodiester bonds, oxime bonds, imine bonds, imide bonds, including any combination thereof.

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74. The method according to claim 73, wherein the chemical bond linking functional entities of two or more building blocks is formed by a reaction of a nucleophile group of a first functional entity with an ester or thioester of another functional entity.

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75. The method according to claim 73, wherein the linker of the building block bearing the thioester group is cleaved simultaneously with the formation of the bonding resulting in a transfer of functional group to the nucleophilic building block.

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76. The method according to claim 74 or 75, wherein the nucleophile group is selected from  $\text{-NH}_2$ ,  $\text{H}_2\text{NHN-}$ ,  $\text{HOHN-}$ ,  $\text{H}_2\text{N-C(O)-NH-}$ .
77. The method of claim 1, wherein the backbone structure of said templated molecule comprises or essentially consists of a molecular group selected from -  
 5  $\text{NHN(R)CO-}$ ;  $\text{-NHB(R)CO-}$ ;  $\text{-NHC(RR')CO-}$ ;  $\text{-NHC(=CHR)CO-}$ ;  $\text{-NHC}_6\text{H}_4\text{CO-}$ ;  
 $\text{-NHCH}_2\text{CHRCO-}$ ;  $\text{-NHCHRCH}_2\text{CO-}$ ;  $\text{-COCH}_2\text{-}$ ;  $\text{-COS-}$ ;  $\text{-CONR-}$ ;  $\text{-COO-}$ ;  $\text{-}$   
 $\text{CSNH-}$ ;  $\text{-CH}_2\text{NH-}$ ;  $\text{-CH}_2\text{CH}_2\text{-}$ ;  $\text{-CH}_2\text{S-}$ ;  $\text{-CH}_2\text{SO-}$ ;  $\text{-CH}_2\text{SO}_2\text{-}$ ;  $\text{-CH(CH}_3\text{)S-}$ ;  $\text{-}$   
 10  $\text{CH=CH-}$ ;  $\text{-NHCO-}$ ;  $\text{-NHCONH-}$ ;  $\text{-CONHO-}$ ;  $\text{-C(=CH}_2\text{)CH}_2\text{-}$ ;  $\text{-PO}_2\text{NH-}$ ;  $\text{-PO}_2\text{-}$   
 $\text{CH}_2\text{-}$ ;  $\text{-PO}_2\text{CH}_2\text{N}^+\text{-}$ ;  $\text{-SO}_2\text{NH-}$ ; and lactams.
78. The method of claim 1, wherein the functional entity is selected from the group of precursors selected from  $\alpha$ -amino acid precursors,  $\beta$ -amino acid precursors,  $\gamma$ -amino acid precursors, and  $\omega$ -amino acid precursors.
79. The method according to claim 1, wherein a functional group of at least one functional entity is linked to another functional entity by means of a bridging molecule.
80. The method according to claim 79, wherein the functional entities are neighbours.
81. The method of claim 1, wherein the templated molecule comprises or essentially consists of at least 2 different functional groups, such as at least 3 different functional groups, for example at least 4 different functional groups, such as at  
 25 at least 5 different functional groups, for example at least 6 different functional groups, such as at least 7 different functional groups, for example at least 8 different functional groups, such as at least 9 different functional groups, for example at least 10 different functional groups, such as more than 10 different  
 30 functional groups.
82. The method of claim 1, wherein each building block comprises at least one reactive group type I.



83. The method according to claim 1, wherein each building block comprises at least one reactive group type II.
- 5 84. The method of claim 82, wherein each building block comprises two reactive groups type I.
85. The method of claim 83, wherein each building block comprises two reactive groups type II.
- 10 86. The method according to claim 85, wherein at least one building block comprises three or more, such as four or more reactive groups type II.
87. The method according to claims 85 or 86, wherein the reactive groups type II are similar.
- 15 88. The method according to claims 85 or 86, wherein the reactive groups type II are reaction partners.
89. The method according to claims 87 or 88, wherein the reactive groups type II are capable of forming a linkage between the functional groups through a bridging molecule.
- 20 90. The method according to claim 89, wherein the bridging molecule is a di-functional compound with reactive groups which are reaction partners to the reactive groups type II of the functional entities.
- 25 91. The method according to claim 85, wherein the reactive groups type II are non-similar.
- 30 92. The method according to claim 91, wherein the non-similar reactive groups type II are reaction partners.
93. The method according to claim 91 or 92, wherein the reactive groups type II are capable of forming a linkage between the functional groups through a bridging molecule.
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- 5 94. The method according to claim 91, wherein the bridging molecule is a di-functional compound with reactive groups which are reaction partners to the reactive groups type II of the functional entities.
- 10 95. The method of any of claims 82 to 94, wherein the at least one reactive group type II of the functional entity is selected from the group consisting of N-carboxyanhydride (NCA), N-thiocarboxyanhydride (NTA), coumarin, amine, carboxylic acid, ketone, aldehyde, hydroxyl, thiol, ester, thioester, alkenyl, any conjugated system of double bonds, hydrazine, N-hydroxysuccinimide ester, and epoxide.
- 15 96. The method of claims 78 to 90, wherein the reactive group type II is an electrophile.
- 20 97. The method according to claim 191, wherein the reactive group type II is an electrophile selected from the group consisting of  $-X-C(O)-R$ ,  $-X-C(O)-CHR-C(O)-R$ ,  $-X-C(O)-CR=CH-R$ , and  $-X-C(O)-CHR-NHR$ , wherein X is a S or O, and R independently is a functional group.
- 25 98. The method of claims 83 to 95, wherein the reactive group type II is a nucleophile.
99. The method according to claim 98, wherein the reactive group type II is a nucleophile selected from the group consisting of  $-NH_2$ ,  $H_2NHN-$ ,  $HOHN-$ , and  $H_2N-C(O,S)-NH-$ .
- 30 100. The method of claims 83 to 95, wherein the reactive group type II is a radical.
101. The method according to any of the preceding claims, wherein the functional entity comprises a reactive group type II connected to the linker.
- 35 102. The method according to claim 101, wherein said functional entity further comprises at least one further reactive group type II.

103. The method according to claim 102, wherein the functional entity comprising the at least one further reactive group type II is capable of forming a link to a second functional entity having a reactive group type II interspaced between said functional entity and the linker, by a reaction involving the reactive group type II on said other functional entity.
104. The method according to claim 103, wherein the link between the second functional entity and the linker is cleaved resulting in a translocation of the functional group of the second functional entity to the first functional entity.
105. The method according to any of the claims 101 to 104, wherein the linkage between the first and the second functional entity is formed by a direct reaction of the respective reactive groups type II.
106. The method according to any of the claims 101 to 104, wherein the linkage between the first and the second functional entity is formed through a bridging molecule.
107. The method according to any of the preceding claims, wherein multiple functional groups are linked by a reaction cascade involving a plurality of building blocks.
108. The method according to any of the claims 101 to 107, wherein multiple functional groups are linked by a reaction cascade involving a plurality of building blocks, each of said building blocks comprising a functional entity which comprises a first reactive group type II connected to the linker, said functional entity comprising at least one further reactive group type II.
109. The method according to any of the preceding claims, wherein the functional entity is restricted as to rotation to obtain a preferred orientation during formation of linkages to other functional entities.

110. The method according to claim 109, wherein one or more bondings that links the functional entity to the complementing element is fixed with regard to rotation.
- 5 111. The method according to any of the claims 109 and 110, wherein the preferred orientation is obtained by coupling the functional entity to the base as well as the (deoxy)ribose moiety of a nucleotide building block.
- 10 112. The method according to any of the claims 109 to 111, wherein the functional entity is coupled to two bases of a dinucleotide.
- 15 113. The method according to any of the preceding claims, wherein the formation of the templated molecule involves the reactive groups type II capable of forming a polymer through anionic, cationic, or radical polymerisation.
- 20 114. The method according to any of the preceding claims, comprising a scaffold functional entity comprising one or more reactive groups type II, said scaffold functional entity being the basic chemical structure for forming a templated molecule by addition of functional groups emanating from the plurality of building blocks.
- 25 115. The method according to claim 114, wherein the scaffold functional entity comprises two or more reactive groups type II.
- 30 116. The method according to claim 114 or 115, wherein the scaffold functional entity is linked covalently to the template.
117. The method according to any of the claims 114 to 115, wherein the scaffold functional entity is linked to a complementing element capable of recognising a coding element of the template.
- 35 118. The method according to any of the claims 114 to 117, wherein building blocks attached to the template comprises functional entities carrying reactive groups type II capable of forming a link to the scaffold functional entity.

119. The method according to any of the claims 114 to 118, wherein a scrambling of linking of functional groups to the scaffold functional entity is obtained by having a different number of reactive groups type II on the scaffold functional entity compared to the number of reactive groups type II on the functional entities of the plurality of building blocks.
120. The method according to any of the claims 114 to 119, wherein the reaction of the reactive groups type II on the scaffold and the corresponding reactive groups type II on the building blocks result in a simultaneous linkage of the functional groups to the scaffold functional entity and cleavage of the linker connecting the functional entity with the complementing element.
121. The method according to any of the preceding claims, wherein a plurality of templates having different coding elements and/or different order of coding elements is used.
122. The method according to claim 121, wherein two or more different templates are used.
123. The method according to claim 121 or 122, wherein four or more different templates, such as more than  $10^3$ ,  $10^5$ ,  $10^7$ ,  $10^9$ ,  $10^{11}$ ,  $10^{13}$ ,  $10^{15}$ ,  $10^{17}$  different templates are used.
124. The method according to claim 121, wherein the plurality of different templates results in a library of different templated molecules, each of said templated molecules being connected to the specific template or complementing template that templated the molecule.
125. The method of any of the preceding claims comprising the further step of releasing the template or complementing template from the templated molecule, and obtaining a templated molecule that is not linked to the complementing template or template that templated the synthesis of the templated molecule.

126. A composition of templated molecules prepared in accordance with any of the claims 121 to 124, wherein said composition comprises a plurality of more than or about  $10^3$  different templated molecules, such as more than or about  $10^4$  different templated molecules, for example more than or about  $10^5$  different templated molecules, such as more than or about  $10^6$  different templated molecules, for example more than or about  $10^7$  different templated molecules, such as more than or about  $10^8$  different templated molecules, for example more than or about  $10^9$  different templated molecules, such as more than or about  $10^{10}$  different templated molecules, for example more than or about  $10^{11}$  different templated molecules, such as more than or about  $10^{12}$  different templated molecules, for example more than or about  $10^{13}$  different templated molecules, such as more than or about  $10^{14}$  different templated molecules, for example more than or about  $10^{15}$  different templated molecules, such as more than or about  $10^{16}$  different templated molecules, for example more than or about  $10^{17}$  different templated molecules, such as more than or about  $10^{18}$  different templated molecules.
127. The composition according to claim 126, wherein said composition further comprises the template capable of templating each templated molecule, or a subset thereof.
128. A composition according to claim 127, wherein the templated molecule is linked to the template capable of templating the templated molecule.
129. The composition according to claim 128, wherein the template molecule is covalently linked to the template.
130. The composition according to claim 128, wherein the templated molecule is linked non-valently to the template.
131. The composition according to claim 130, wherein the non-covalent linkage involves one or more bondings selected from the group consisting of hydrogen bondings, van der Waals bondings, and ionic bondings.

132. The composition according to claims 126 to 131, wherein the templated is prepared in accordance with claim 1 to 125, where said templated molecule is bound to another molecule selected from the group consisting of DNA, RNA, antibody, peptide, or protein, or derivatives thereof.

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133. A method for screening a composition of molecules having a predetermined activity comprising:

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i) establishing a first composition of templated molecules, said composition of templated molecules being as defined in any of the claims 126 to 132, or produced as defined in any of the claims 1 to 125,

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ii) exposing the first composition to conditions enriching said first composition with templated molecules having the predetermined activity, and

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iii) optionally amplifying the templated molecules of the enriched composition obtaining a second composition,

iv) further optionally repeating step ii) to iii), and

v) obtaining a further composition having a higher ratio of templated molecules having the specific predetermined activity.

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134 The method of claim 133, further comprising a step of mutating the templated molecules, wherein said mutagenesis can take place prior to carrying out step iii), simultaneously with carrying out step iii), or after carrying out step iii).

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135 The method of claim 134, wherein the mutagenesis is carried out as random or site-directed mutagenesis.

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136 The method of claim 133, wherein step iii) comprises a  $10^1$  to  $10^{15}$ -fold amplification.

137 The method of claim 133, wherein the steps ii) and iii) are repeated at least 2, 3, 5 times, such as at least 10 times, such as at least 15 times.

5 138 The method of claim 133, further comprising a step of identification of the templated molecule having the predetermined activity.

10 139 The method of claim 133, wherein the identification is conducted by analysing the template and/or complementary template physically or by other means associated with the molecule.

15 140 The method of claim 133, wherein the conditions enriching the composition comprises providing a binding partner to said templated molecule having the predetermined activity, said binding partner being directly or indirectly immobilised on a support.

20 141 The method of claim 133, wherein the conditions enriching the composition involves any one or more of electrophoretic separation, gelfiltration, immunoprecipitation, isoelectric focusing, centrifugation, and immobilization.

25 142 The method of claim 133, wherein the predetermined activity is an enzymatic activity or a catalytic activity.

30 143 The method of claim 133, wherein the conditions enriching the composition comprises providing cells capable of internalising the templated molecule, or performing an interaction with the templated molecule having the predetermined activity.